

Introduction

The life form which exists without a cellular structure is known as **acellular** or non-cellular life. The primary candidates for non-cellular life are viruses. Majority of biologists consider viruses are non living because they are not capable of **autopoiesis** (ability of reproduction) without host. The other examples of acellular life are **viroids** which are smallest infectious agents consisting solely of short strands of circular single stranded RNA without protein coat. The **prions** are infectious agents composed entirely of protein, capable of multiplying itself and transferable from one host to another.

5.1 Viruses Discovery and Structure

A virus is a biological agent that reproduces only inside the cells of living host. Viruses can infect all type of life forms i.e., from animals and plants to microorganisms including bacteria.

In 1884 the French microbiologist **Charles Chamberland** made a filter paper for filtration of bacteria. In 1892, Russian biologist **Ivanovsky** used this filter to determine the cause of **tobacco mosaic disease**. In his experiment he proved that tobacco mosaic disease was not caused by bacteria but caused by other infectious agent which can pass through filter paper. He called these filterable viruses. His view was confirmed by American virologist **W.M. Stanley in 1935**, when he observed tobacco mosaic virus under Electron Microscope.

In the early 20th century (1915, 1917) **Twort and Herelle** discovered bacteriophages (viruses that infect bacteria). Since then thousands of species of viruses have been discovered and microbiologists speculate that there are millions of species of viruses still to be discovered.

5.1.1 Viruses Living or Non Living

Viruses show the characteristics of both living and non-living things. The **living characteristics** of viruses include:

- They have their own genetic material.
- They undergo mutation.
- Can reproduce inside host cell by using host metabolic machinery.
- Get destroyed by ultraviolet radiations and chemicals.
- Occur in different varieties or strains.

The **non-living characteristics** of viruses include:

- They are non-cellular particles.
- Generally lack enzymes and co-enzymes and depend upon host enzymes and coenzymes for their metabolic activities.
- Can be crystallized and stored in laboratory.
- Do not respire and use the energy of host for their activities.
- Therefore, depending upon the ambivalent(fluctuating) nature of characteristics possessed by the Viruses; they are considered on **boundary line between living and non living things**.

5.1.2 Classification of Viruses

Viruses may be classified on the basis of morphology, type of host they infect, presence or absence of outer covering and types of nucleic acid.

Classification of viruses based upon structure (morphology):

1. On the basis of capsid:

- Some viruses have helical capsid such as tobacco mosaic virus (TMV).
- Many have polyhedral capsid, contain a glycoprotein spike at each vertex, such as adenovirus.
- Viruses possess an outer envelope studded with glycoprotein spike, such as Influenza viruses.
- Viruses like bacteriophage possess complex capsid consisting of a polyhedral head and tail apparatus.

2.

On the basis of genome (DNA and RNA):

Double stranded DNA viruses (dsDNA Viruses).
e.g., Adenoviruses, Herpes viruses, Pox viruses.

Single stranded DNA viruses (ssDNA Viruses),
e.g., Paroviruses (small viruses of vertebrates and invertebrates) cause rash.

Double stranded RNA viruses (dsRNA viruses),
e.g., Reoviruses, cause diarrhoea.

Single stranded RNA reverse transcribing viruses template for DNA (ssRNA-RT viruses), e.g., HIV (retrovirus).

Do you know?



Bacteriophages are ubiquitous viruses found wherever bacteria exist. It is estimated that number of Bacteriophages is more than any other organism on earth.

Classification of viruses on the basis of host they infect:

Bacteriophages attack bacteria.

Plant viruses which cause more than 2,000 types of plant diseases such as TMV, Potato yellow dwarf virus.

Animals viruses cause many diseases to animals and human such as mouth and foot disease in livestock, papovavirus causes mumps and measles. Rous sarcoma virus causes cancer.

5.1.3 Structure of Model Viruses

A virus particle (virion) consists of nucleic acid core surrounded by a protective coat of protein called capsid. The nucleic acid found in viruses is either DNA or RNA but

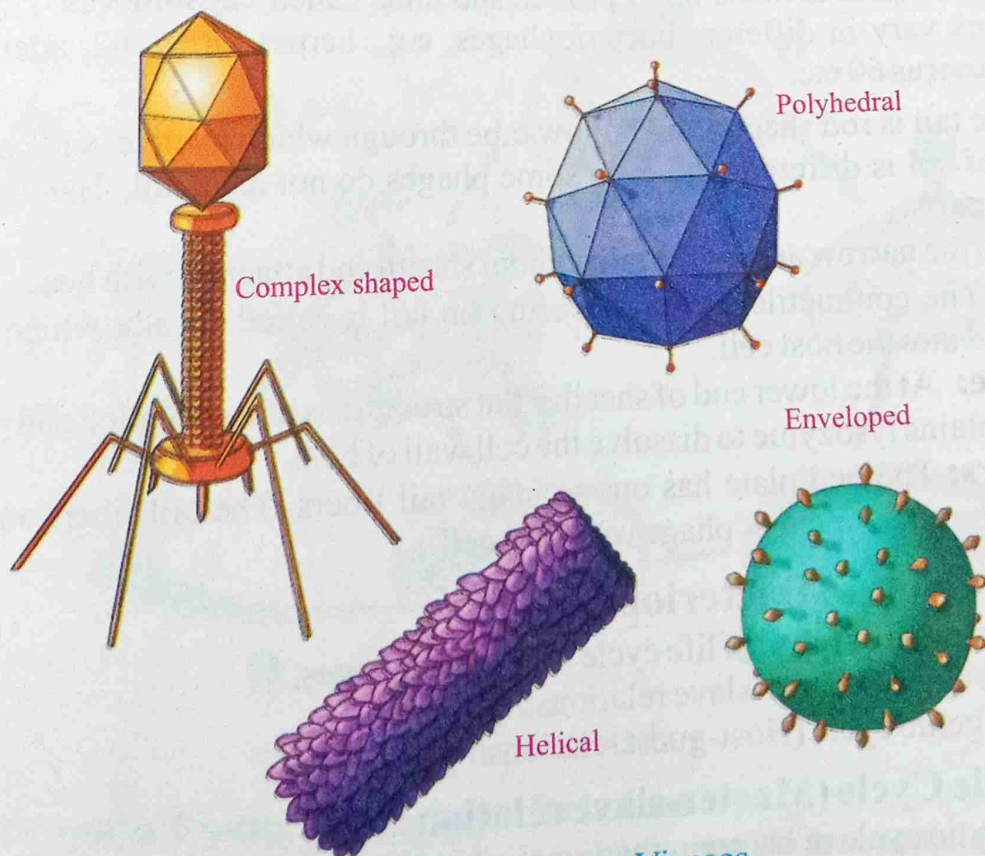


Fig. 5.1 Shape of some Viruses

not both. The **capsid** is made of many smaller, identical protein molecules called **capsomeres**. Their number and arrangement varies in different types of viruses. Some viruses have an **envelope** of lipid outside the protein coat. This envelope is derived from host cell and such viruses which have envelope are called enveloped viruses. The viruses have different shapes like enveloped, tadpole or complex shaped, polyhedral, spherical, helical etc.

Structure and life cycle of some viruses (Bacteriophages, flu virus and HIV):

5.1.4 Structure of Bacteriophage

A Bacteriophage is a virus that infects and replicates within a bacterium. They vary in size from 24 to 200 nm in length. A bacteriophage consists of two main parts, i.e., head and tail.

Head: The head (nucleocapsid) is further divided into two parts, inner core of nucleic acid and outer coat of protein. The nucleic acid may be mostly DNA, however, some have RNA. The number of genes in a bacteriophage genome vary from few to over 100.

The protein coat or capsid of bacteriophage is usually **hexagonal** like prism shaped. The capsid is made up of protein sub units called **capsomeres**. The number of capsomeres vary in different bacteriophages, e.g., herpes virus 162, adenovirus 252, ambidensovirus 60 etc.

Tail: The tail is rod shaped and hollow tube through which nucleic acid passes in host. The size of tail is different and even some phages do not have tail. The tail consists of following parts.

Neck: It is the narrow area of the tail without sheath and attached with head.

Sheath: The contractile protein covering on tail is called sheath, which pushes the nucleic acid into the host cell.

Base Plate: At the lower end of sheath a flat structure is present called end plate or basal plate. It contains lysozyme to dissolve the cell wall of host.

Tail Fibers: The end plate has one to many tail fibers. The tail fibers and base plate involve in the attachment of phage with host cell.

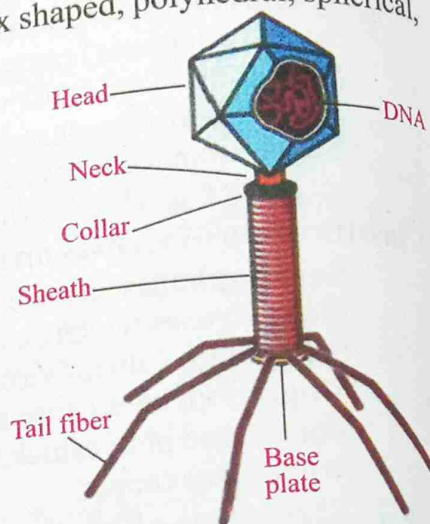


Fig. 5.2 Bacteriophage

5.2 Life Cycle of Bacteriophage

There are two types of life cycle of bacteriophages.

- Lytic cycle (Master-slave relationship)
- Lysogenic cycle (Host-guest relationship)

5.2.1 Lytic Cycle (Master-slave relationship)

The lytic cycle of bacteriophage consists of following steps.

5.2.3 Influenza or Flu Virus

It is an RNA enveloped virus, belongs to family orthomyxoviruses. It includes seven genera but out of seven three genera usually cause influenza in humans and some other vertebrates. These three genera are influenza virus A, influenza virus B and influenza virus C. Each genus include only one species, i.e., influenza A, B and C virus.

The **influenza A** and **C** cause infection in different vertebrates including humans but **influenza B** almost exclusively infects human.

Vaccines and drugs are available for the treatment of influenza virus infection but flu viruses develop resistance against these vaccines and drugs. Therefore, vaccines and drugs have to be reformulated regularly.

Human Immunodeficiency Virus (HIV):

Human immunodeficiency virus (HIV) is an RNA enveloped virus. It is spherical in shape. It is a retrovirus, i.e., it can convert its RNA into DNA in host cell. It causes acquired immunodeficiency syndrome (AIDS) in humans. It belongs to family retroviridae and genus lentivirus.

Structure of HIV:

It is roughly spherical in shape, about 120 nm in diameter. HIV consists of two strands of RNA enclosed by a conical capsid. The capsid is surrounded by an envelope.

The envelope is formed when the capsid buds off from host cell, taking some of the host cell membrane with it. The envelope contains glycoprotein receptors responsible for binding to and entering the host cell. Several enzymes like reverse transcriptase, protease and integrase are also present.

Do you know?



The total genome length of flue virus is 12000-15000 nucleotides and the genome contains 6-8 segments or pieces of varying lengths.

Symptoms of influenza

include fever, shivering, dry cough, chill, loss of appetite, body-ache, nausea, irritation in throat and nose etc.

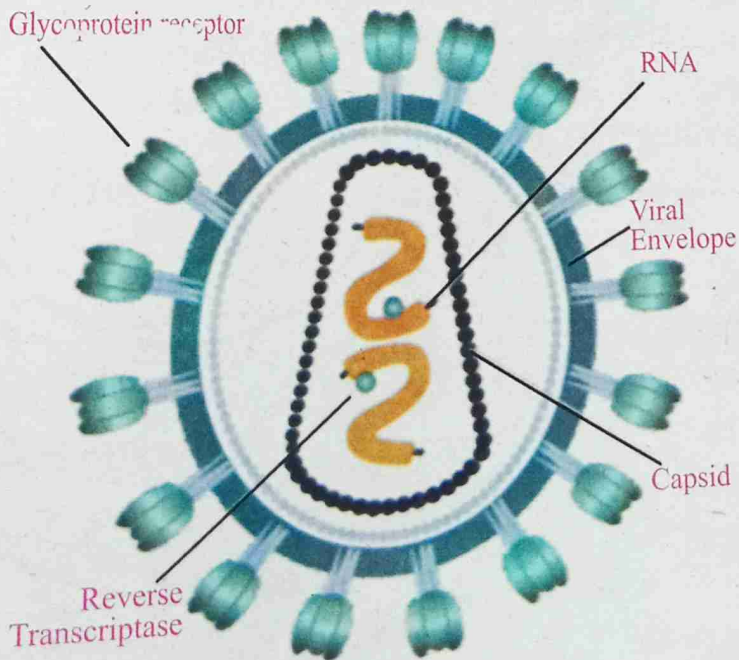


Fig. 5.5 Structure of HIV

5.3 Discovery of HIV

HIV causes AIDS (Acquired immunodeficiency syndrome). The HIV was first identified in 1984 in France and USA. The name HIV (Human immune deficiency virus) was given to this virus in 1986. HIV attacks on some special type of white blood cells (macrophages, lymphocytes). These cells are known as T4 cells and are the primary hosts of HIV.

5.3.1 Life cycle of HIV (How does HIV recognize T4 cells?)

The HIV has glycoprotein receptors on its envelope while T4 cells have CD4 (Cluster of differentiation) receptor, during travelling in blood HIV glycoprotein receptors stick with T4 cells on CD4 protein receptors.

Once HIV binds to a host cell, the viral envelope fuses with the cell membrane, the RNA and enzymes of virus enter into the host cell. Three types of enzymes of HIV which come into host cell along with RNA are reverse transcriptase, integrase and protease. The reverse transcriptase converts viral RNA into DNA. The enzyme **integrase** then facilitates the delivery of this viral DNA into the host DNA.

Tit bits

HIV screening test is done by ELISA. However, ELISA test is relatively less authentic, so PCR test is recommended which is more authentic.

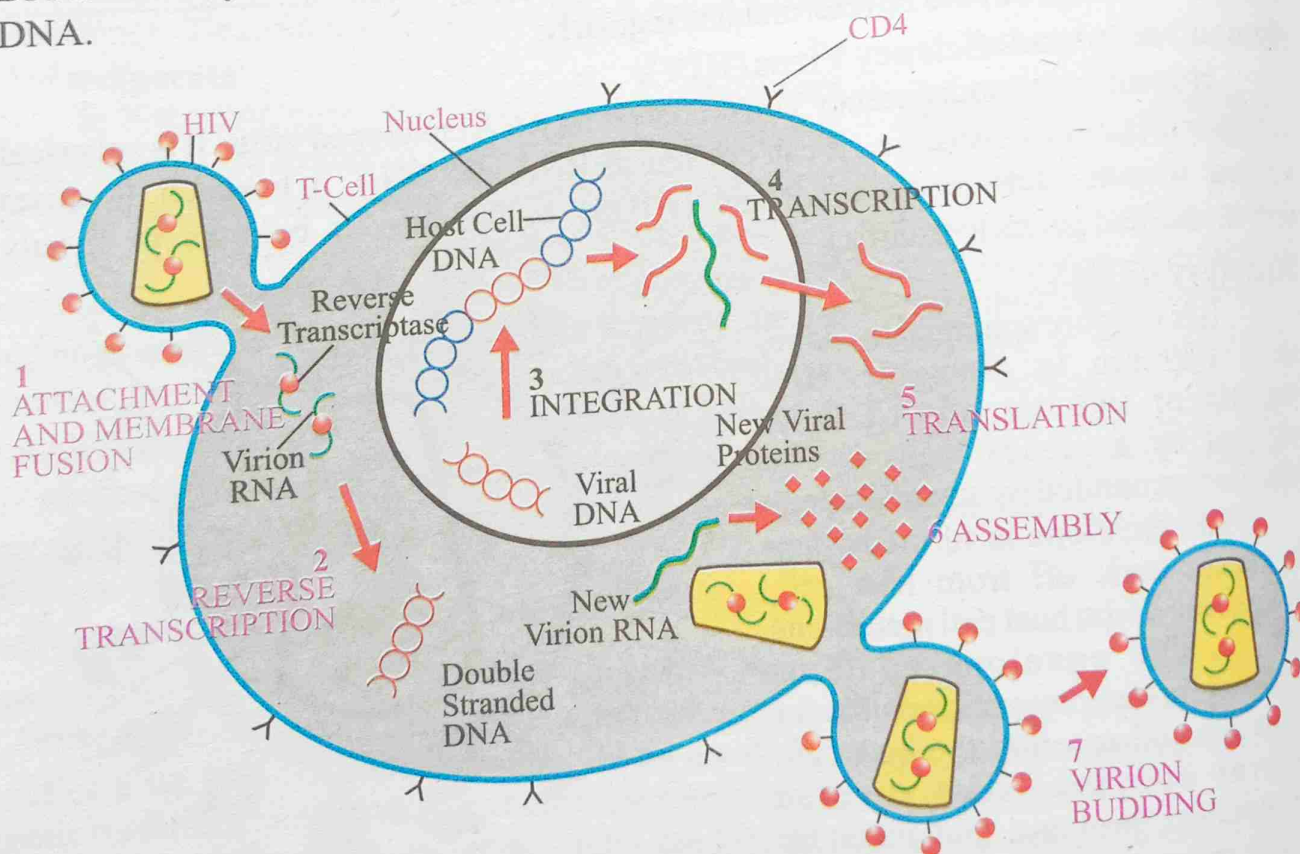


Fig. 5.6 Life cycle of HIV

The integrated DNA is now called provirus. Virus mRNA is transcribed in host cell by host cell polymerase. This mRNA is translated into proteins. These proteins are large in size which are then cleaved by the protease enzyme to form virion structural proteins. Thus immature virion is produced which is budded off from cell membrane. As it buds off, it takes the covering of host cell membrane and becomes mature infectious virion. A cell infected with retrovirus does not necessarily lyse the cell when its replication takes place. In HIV infection T4 cells are destroyed thus immunity is decreased and patient becomes susceptible to other diseases. As it causes immune system deficiency so it was called HIV (Human Immunodeficiency virus).

Symptoms of AIDS:

The infection of HIV may be divided into three stages. **The first stage** is known as primary infection. In this stage symptoms like fever, swollen lymph nodes, inflammation of throat, night sweating occur. However, these symptoms disappear after some days and there are no symptoms for about nine months, therefore, this first stage is called **asymptomatic carrier**.

The second stage known as **AIDS related complex**. In this stage some of early symptoms of acute infection reappear like swollen lymph nodes under the armpit, neck region, groin region, fever, aches etc. Some other symptoms like persistent cough, persistent diarrhoea, flu, night sweating, loss of memory, loss of judgment and depression, weakness etc. This stage may continue from few months to many years.

The last stage of HIV infection is called **full blown AIDS**. This stage is characterized by severe weight loss, weakness and opportunistic infections such as **kaposi's sarcoma** (skin cancer), **cervical cancer** and **cancer of lymphatic system**. Opportunistic infections are such infections which are caused by very weak pathogens which usually never cause infection as our immune system can easily destroy them.

Transmission of AIDS:

The HIV is transmitted by three main routes i.e., sexual contact, body fluids and mother to child.

The sexual contact is most frequent cause of HIV transmission. The second most common mode of HIV transmission is **body fluid**, it includes blood transfusion, surgical instruments, contaminated syringes, razors, blades etc. **The mother to child** transmission may occur during pregnancy, during delivery or breast feeding.

Prevention of AIDS:

There is currently no cure or vaccine to prevent or cure HIV infection. A treatment

Tit bits

There are two species of HIV, i.e., HIV-I and HIV-II. HIV-I is most common pathogenic strain while HIV-II is not widely recognized outside Africa.

Red Ribbon

The red ribbon is a symbol for solidarity with AIDS patients.



World AIDS Day

1st December is world AIDS Day, it is being observed every year since 1988. It is dedicated to raising awareness about AIDS prevention.



known as **highly active antiretroviral therapy (HAART)** is given but no significant improvement is observed. Therefore, prevention is the only cure for AIDS. The following **preventive measures** are recommended to avoid HIV infection.

- i) Avoid immoral sexual contacts and follow Islamic teachings in order to live clean and healthy life.
- ii) Surgical instruments must be sterilized before use.
- iii) Disposable syringes should be used. Blood must be screened before transfusion.
- iv) Do not share razor blades and tooth brushes.
- v) HIV positive mothers should avoid breast feeding.

5.4 Parasitic Nature of Viruses

Viruses are obligate parasites i.e., they cannot reproduce and live outside living cells. It is because viruses lack metabolic enzymes, ribosomes, mitochondria etc for making protein and energy. Therefore, viruses must need a host cell for their life cycle.

Viruses are highly specific with respect to their hosts, e.g., HIV attacks on T4 cells of human. Polio virus infects spinal nerve cells. Hepatitis virus attacks on liver cells. Bacteriophages attack only bacteria etc. However, some viruses have a broad range of specificity e.g., rabies virus can infect all mammalian cells.

When any foreign agent enters inside the body it is destroyed or killed by macrophages and neutrophils or antibodies produced by Bursa lymphocytes. But in some capsule, protein and fibrin do not bind by gag (swing) like substances secreted by Bursa lymphocytes which are used by macrophages and neutrophils. That is why viruses are saved from being phagocytized. Some viruses cover with host proteins, therefore, body immune system is unable to detect them as foreign body and they remain protected. Many viruses continuously change their shape and appearance as a result body immune system and vaccine becomes ineffective against new types, e.g., influenza and HIV viruses also remain safe in the body when immune system gets weak as in AIDS.

How viruses tolerate unfavorable conditions outside host cell?

Outside the host cell viruses are changed into crystals. In crystal form they are seen dead and show no activities. Upon reaching the host cell, i.e., in favorable condition they become active again and start reproducing by using host enzymes and proteins. The crystals of viruses may be present in saliva, respiratory droplets, feces etc.

5.5 Viral Diseases

A disease caused by virus is known as viral disease. Viruses cause number of diseases in plants, animals and human beings. A brief introduction of some viral diseases is given below.

Hepatitis:

Hepatitis is the inflammation of liver (Gk. *Hepa* = Liver, *itis* = inflammation).

There are different causes of hepatitis such as alcohol, drugs and toxins. However, hepatitis is mostly caused by viral infections. There are several types of viral hepatitis like A, B, C, D and E.

Hepatitis A: It is caused by RNA virus called HAV. The HAV is non-enveloped icosahedral shaped virus which cause a mild, short term disease. It is transmitted by contact with feces from infected person and drinking sewage contaminated water.

Vaccine is available for the prevention of HAV but no antiviral therapy is available.

Hepatitis B: Serum Hepatitis: It is caused by DNA enveloped virus called HBV. It is transmitted by blood, sexual contact, contaminated blood transfusion and by infected mothers to their babies, saliva etc. It may cause liver cirrhosis and death if not treated timely. The vaccine for HBV is available. **Alpha interferon** and some nucleoside analogues are effective treatment for HBV.

Hepatitis C: It is caused by RNA enveloped virus called HCV. It is a chronic and fatal disease, may cause cirrhosis, hepatocellular carcinoma and death if left untreated. The mode of transmission is via blood, sexual contact, breast feeding, sharing needles, tooth brushes etc. No vaccine is available for HCV, however, antiviral therapy is available usually a combination of interferon and ribavirin is given to the patients.

Hepatitis D: It is caused by HDV also called delta virus. This virus is only active in the presence of HBV, so it can be treated or prevented by treating HBV. Its mode of transmission is also same as HBV. It is small spherical enveloped viroid.

Hepatitis E: It is caused by HEV. It is non-enveloped single stranded RNA virus. The symptoms of HEV are similar to HAV. But it can be more fulminant in some cases such as pregnancy. No vaccine or antiviral drugs available.

Herpes: There are two types of herpes viruses which cause herpes, i.e, herpes simplex virus I and II. These are double stranded DNA viruses having large genome covered with protein coat and envelope. Herpes simplex-I is known as cold sore while herpes simplex-II is known as genital herpes. Herpes-I is transmitted by saliva while herpes-II is transmitted by sexual contact. The symptoms include water blisters in the skin or mucous membranes of mouth, lips, nose, genitals and skin lesions. Herpes can be treated by using antiviral drugs and may be prevented by avoiding sexual contacts and physical contacts with infected persons.

Poliomyelitis (infantile paralysis)

It is highly infectious viral disease that can lead to paralysis, breathing problem or even death. This virus was first identified by Karl Landsteiner in 1908. Primarily, it is

Tit bits

Polio virus is usually spread by infected fecal matter entering the mouth. It may also spread by food and water contaminated by feces or saliva.

Tit bits

Polio has been almost eradicated from world. However, Pakistan, Afghanistan and Nigeria are the countries where polio cases are identified.

transmitted by contaminated water of infected fecal material but may also be transmitted by sneezing and coughing. There are many different symptoms of polio. These symptoms may be divided in two types.

- i) **Non-paralytic polio symptoms:** These include flu, weakness, fever, sore throat, headaches, vomiting, fatigue, muscle tenderness etc.
- ii) **Paralytic polio symptoms:** These include loss of muscle reflexes, severe muscle pain spasm and damage to motor nerve etc.

There is no cure for polio, however, it can be prevented by vaccination. Two types of polio vaccines are available, i.e., inactivated polio vaccine (IPV) and oral polio vaccine (OPV).

Leaf Curl Virus Disease

Leaf curl is a plant disease characterized by curling of leaves, darken veins and veins swellings. The disease mainly affects the cotton plant which is one of the most important crop of Pakistan, accounting for over 60% of foreign exchange earnings.

In Pakistan this disease was first reported in Punjab region near the city of Multan in 1985. Now it is spread in other parts of Pakistan and the neighbouring countries. It is a main threat to cotton crop. It is caused by a cotton leaf germinivirus (CLCuV). The vector of this virus is whitefly *Bemisia tabaci*. Therefore, this disease can be prevented by protecting the cotton seedlings from the attack of whiteflies. The infected plants should be burnt and healthy seeds should be used for sowing.

Bird Flu in Pakistan

Bird flu is also called avian influenza. It is a viral infection that can infect not only birds but also humans and other animals. However, most forms of virus are restricted to birds.

H_5N_1 is the most common form of bird flu. It is deadly disease of birds and it can also easily affect humans and other animals that come in contact with infected birds. H_5N_1 are capable to survive for long

Tit bits

Prions have different structure than normal protein of body. Therefore, they are resistant to protease enzyme.



Fig. 5.7 Cotton Leaf Curl Disease



Fig. 5.8 Birds infected from birds flu virus

Activity

Relate enzyme activity with antibiotics by searching internet and find out the reason why antibiotics are not effective against viruses.

5.6 Prions

Prions are proteinaceous infectious particles which cause transmissible neurodegenerative disease. Stanley in 1982 discovered these particles. The prions affect the nervous system of human and other mammals.

The transmission of prion is mainly by unhygienic way of feeding, contaminated food. Some prions diseases of human are **creutzfeldt Jacob disease (CJD)**, **kuru**, **fatal familial insomnia (FFI)**. These diseases are caused by eating beef products obtained from cattle with prions diseases. **Scrapie** is a common disease of bovine caused by prion. It is also known as **mad cow disease**. Loss of memory, paralysis, destruction of nerve tissues are symptoms of prion disease. No effective treatment is available and illness is progressive and always fatal.

Viroids

Viroids are single molecules of circular RNA without a protein coat or envelope so they are called simple RNA. These are smaller in size than virus, ranging from 246-270 nucleotides.

Viroid was first discovered by T. O. Diener in 1971. Viroids cause diseases in plants such as **potato spindle tuber disease**, **cucumber pale fruit**.

The mechanism of viroids replication is unclear so far.

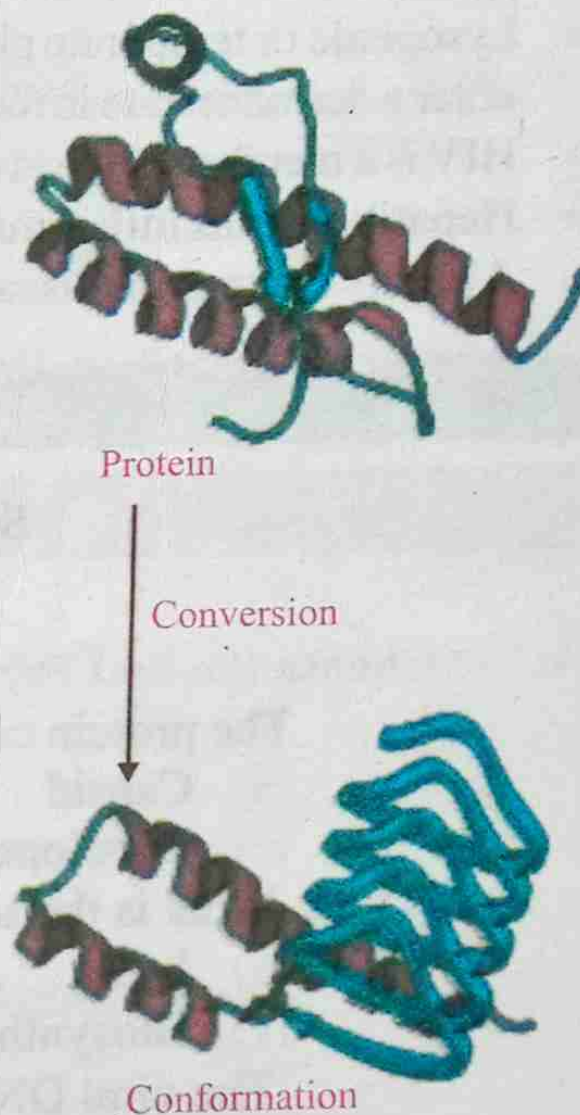


Fig. 5.9 Structure of Prion

EXERCISE

Section I: Objective Questions

Multiple Choice Questions

Choose the best correct answer.

1. The protein coat of a virus is called the:
(a) Capsid (b) Capsomere
(c) Envelope (d) Viral membrane
2. What is the second step of bacteriophage infection
(a) Lysis (b) Attachment
(c) Biosynthesis (d) Penetration
3. The viral DNA incorporated into a lysogenic cycle is called.
(a) Prophage (b) Latent phage
(c) Bacteriophage (d) Oncogenic virus
4. Prions cause disease by
(a) Altering normal proteins (b) Altering genes
(c) Activity of a reverse transcriptase (d) Produce poison

5. What type of infectious agent causes potato spindle tuber disease?
 - (a) Prion
 - (b) Virino
 - (c) Viroid
 - (d) Virus
6. Prion diseases can be acquired in all of the following ways except by
 - (a) Transplantation
 - (b) Inherited
 - (c) Direct contact
 - (d) Ingestion
7. Carbohydrate-protein complexes that project from the surface of some viruses are
 - (a) Caspid
 - (b) Capsomeres
 - (c) Envelope
 - (d) Spikes

B. Fill in the blanks.

1. Prions are infectious particles which are composed of only _____.
2. Viroids consist of only a single molecule of circular _____ without protein coat.
3. Polio virus is transmitted by the _____.
4. Master-slave relationship of bacteriophage is called _____ cycle.
5. Host-guest relationship of bacteriophage is called _____ cycle.
6. The tail of phage secretes an enzyme named _____.
7. HEV is non enveloped single stranded _____ virus.

Section II: Short Questions.

Write short answers.

1. What is meant by an obligate intracellular parasite?
2. What is the capsid?
3. What is an enveloped virus, and how does the envelope arise?
4. Write short note on prion.
5. Define bacteriophages and explain their structure.
6. What is necessary for adsorption?
7. What is a prophage or temperate phage?
8. What is the principal effect of the agent of Creutzfeldt-Jakob disease?
9. What are viroids?
10. Why the viral diseases are more difficult to treat than bacterial diseases?

Section III: Extensive Questions.